REMARKS

Claims 13-16, 22-26, and 31-69 are pending. Favorable reconsideration is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, first paragraph, is respectfully traversed.

Independent Claims 15, 38, and 68 recite a DNA which is hybridizable under specified stringent conditions.

The Synopsis of Application of Written Description Guidelines (Guidelines) explicitly states that a claim may recite hybridization conditions and satisfy the written description requirement of 35 U.S.C. §112, first paragraph. Applicants submit herewith a copy of Federal Register, Vol. 63, No. 114, 32642, and Example 9 of the Guidelines. Example 9 explicitly describes an example of a claim which recites stringent hybridization conditions in the claims and satisfies the written description requirement of 35 U.S.C. §112, first paragraph.

Since independent Claims 15, 38, and 68 recite a DNA which is hybridizable under specified stringent conditions, Applicants submit that those claims, and claims dependent thereon, satisfy the requirements of 35 U.S.C. §112, first paragraph, for the reasons set forth in the Guidelines.

Newly-added independent Claim 69 is directed to a method of producing a polypeptide which is defined in terms of sequence and physical properties. Claim 69 certainly satisfies the requirements of 35 U.S.C. §112, first paragraph.

Based on the foregoing, the pending claims satisfy the requirements of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Regarding the obviousness-type double patenting rejection over U.S. 6,166,292, Applicants request that this rejection be held in abeyance until an indication of allowable subject matter in the present application. If necessary, a Terminal Disclaimer will be submitted at that time.

Regarding the claim for priority, Applicants note that a certified copy of the Japanese priority application was filed in the parent application. Therefore, Applicants request an indication of the same in the next communication from the Office.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is respectfully solicited.

Respectfully submitted,

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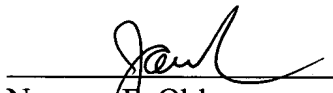

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Docket No.: 195378US0DIV
Serial No.: 09/675,208

Marked-Up Copy
Serial No: 09/675,208
Amendment Filed on:
HEREWITH

IN THE CLAIMS

--13. (Amended) [An isolated DNA encoding a raffinose synthase having] The DNA of claim 15, wherein the polypeptide having the ability to produce raffinose from sucrose and galatinol has the following properties:

(1) [action and substrate specificity: the raffinose synthase produces raffinose from sucrose and galactinol;

(2)] optimum pH: the [raffinose synthase] ability has an optimum pH of about 6 to 8;

[(3)] (2) optimum temperature: the [raffinose synthase] ability has an optimum temperature of about 35 to 40°C;

[(4)] (3) molecular weight: the [raffinose synthase] polypeptide has:

(i) a molecular weight of about 75 kDa to 95 kDa estimated by gel filtration chromatography;

(ii) a molecular weight of about 90 kDa to 100 kDa estimated by polyacrylamide gel electrophoresis; and

(iii) a molecular weight of about 90 kDa to 100 kDa estimated by SDS-polyacrylamide gel electrophoresis under a reduced condition; and

[(5)] (4) inhibition: the [raffinose synthase] ability is inhibited by iodoacetamide, N-ethylmaleimide, and myo-inositol.

14. (Amended) The DNA of Claim 13, [which] wherein the [raffinose synthase] polypeptide comprises an amino acid sequence shown in SEQ ID NO: 1, 2 or 3.

15. (Amended) An isolated DNA encoding a [raffinose synthase] polypeptide having an ability to produce raffinose from sucrose and galatinol, wherein the DNA is hybridizable under stringent conditions to a DNA comprising nucleotide numbers 56 to 2407 of SEQ ID NO: 4, the stringent conditions being 1 x SSC, 0.1% SDS at 60°C.

22. (Amended) [An isolated DNA encoding a raffinose synthase, wherein the DNA is obtained from] The DNA of claim 37, wherein the plant is a dicotyledonous plant.

Claims 37-69 (New).--

D. For Each Claimed Genus, Determine Whether There is Sufficient Written Description to Inform a Skilled Artisan That Applicant was in Possession of the Claimed Genus at the Time the Application was Filed

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by relevant identifying characteristics, i.e., structure or other physical and/or chemical characteristics, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" requires that the species which are expressly described be representative of the entire genus. Thus, when there is substantial variation within the genus, it may require a description of the various species which reflect the variation within the genus. For example, a broadly drawn claim to a specific gene from ruminant mammals may require a representative species from cattle, buffalo, bison, goat, deer, antelope, camel, giraffe and llama.

What constitutes a "representative number" is an inverse function of the predictability of the art, as determined in IIA above. The number must be sufficient to reasonably identify the other members of genus. In an unpredictable art, adequate written description of a genus *cannot* be achieved by disclosing only one species within the genus. In fact, if the members of the genus are expected to vary widely in their identifying characteristics, such as structure and activity, written description for each member within the genus may be necessary.

Generalized descriptions alone, such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," fail to satisfy the written description requirement because they do not describe any members of the genus except by function without any known or disclosed correlation between function and structure.[24] If the correlation between structure and function in the art would not have been known to one skilled in the art and the specification does not describe the correlation, the written descriptive support cannot depend on that correlation.

For each claim to a genus:

(1) Determine whether a representative number of species have been described by complete structure as in C(1) above. If a representative number have been so described, then the applicant has written description support for the claimed genus and a rejection under 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim to a genus:

An isolated DNA probe for detecting HIV-X, wherein said DNA probe hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under the following conditions: hybridization in 7% sodium dodecyl sulfate (SDS), 0.5M $NaPO_4$ pH 7.0, 1mM EDTA at 50° C.; and washing with 1% SDS at 42° C.

In this case, the specification discloses the sequence of the isolated DNA molecule consisting of SEQ ID NO: 1 and discloses several sequences that hybridize to SEQ ID NO: 1. Hybridization under the stringent conditions specified here requires that the claimed nucleic acid probes be structurally similar to the complement of the nucleic acid sequence disclosed as SEQ ID NO: 1. In this case, the description as a whole is sufficient to evidence possession of the claimed genus because the genus is defined by relation to the structure of the sequence provided as SEQ ID NO: 1, and because several species are disclosed that possess the hybridization property which further defines the genus. Thus, this claim to a genus meets the D(1) criteria.

(2) For each claim to a genus not supported as described under D(1), determine whether there is a representative number of adequately described species, as analyzed under C(2). The representative number must permit one skilled in the art to reasonably identify the remaining members of the genus. If a representative number are so described, then the written description requirement is satisfied and, again, a rejection under 112 ¶ 1 for lack of written description must not be made.

For example, consider the following claim to a genus:

A monoclonal antibody which specifically binds to the novel cancer associated TAG-31 antigen but which does not substantially bind normal adult human tissues, wherein said monoclonal antibody has a binding affinity of greater than 3 times 10^9 M^{-1} for TAG-31.

Considering the claim as a whole, it is drawn to a genus of monoclonal antibodies. Although the specification does not disclose the complete structure of a representative number of species to support the claimed genus of antibodies, it does disclose multiple monoclonal antibodies which have the isotype claimed as well as the binding specificity and binding affinity characteristics recited in the claims. In this well-developed art, additional identifying characteristics f r a substantial portion of the genus are well-known (e.g., number of chains, disulfide bonds, constant and variable regions, etc.). Thus, applicant's disclosure combined with what was known in the art are sufficient to describe the claimed genus of monoclonal antibodies in such full, clear, concise and exact terms to show applicant was in possession of th claimed antibodies. Thus, the claim meets the D(2) criteria.

As another example, consider the following claim to a genus:

An isolated mutanase enzyme produced by Bacillus having the following physicochemical properties (1) to (9): (1) action: an ability to cleave alpha-1,3-glucosidic links of mutan; (2) substrate specificity: an ability to effectively decompose mutan; (3) optimum pH: pH 4 to 4.5 when reacting on a mutan substrate at 35 degrees C for 10 minutes; (4) pH range for stability: pH 4 to 10 when kept at 25 degrees C for 24 hours; (5) optimum temperature: 50 degrees to 65 degrees C when reacted at pH 5 with mutan as a substrate; (6) thermal stability: enzyme activity remains stable below 50 degrees C after incubation at pH 5 for 10 minutes; (7) effect of metal ions: mercury and silver show inhibitory effect on a mutan substrate; (8) effect of inhibitors: p-chloromercurybenzoic acid shows inhibitory effect on a mutan substrate; and (9) molecular weight: about 140,000 to about 160,000 as determined by SDS-polyacrylamide gel electrophoresis.

Considering the claim as a whole, it covers a genus of mutanase enzymes. Although the specification does not disclose the complete structure of a representative number of species to support the claimed genus of enzyme compositions, it does disclose 3 mutanase species produced by different strains of Bacillus (mutanases A, B and C) which are identified by multiple relevant identifying characteristics, i.e., molecular weight, substrate specificity, optimum and ranges of temperature and pH for mutan cleavage activity, etc. In this well-developed art, these identifying characteristics are sufficient for a skilled artisan to recognize applicant had possession of the species from the identifying characteristics f the three mutanase species, to reasonably predict sufficient identifying characteristics of the other members of the genus and, thus, establish possession of the genus. Thus, the claim meets the D(2) criteria.

As another example, consider the following claim to a genus:

e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO: 2).

Weighing all factors including (1) that the full length ORF (SEQ ID NO: 2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO: 2.

Conclusion: The written description requirement is satisfied.

Example 9: Hybridization

Specification: The specification discloses a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The specification includes an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of nucleic acids that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1.

Claim:

An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1,

wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

Analysis:

A review of the full content of the specification indicates that the essential feature of the claimed invention is the isolated nucleic acid that hybridizes to SEQ ID NO: 1 under highly stringent conditions and encodes a protein with a specific function. The art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing.

The claim is drawn to a genus of nucleic acids all of which must hybridize with SEQ ID NO: 1 and must encode a protein with a specific activity.

The search of the prior art indicates that SEQ ID NO: 1 is novel and unobvious.

There is a single species disclosed (a molecule consisting of SEQ ID NO: 1) that is within the scope of the claimed genus.

There is actual reduction to practice of the disclosed species.

Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of

skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Conclusion: The claimed invention is adequately described.